REVISED

U.S. EPA HIGH PRODUCTION VOLUME CHEMICAL VOLUNTARY TESTING PROGRAM

TEST PLAN

ISODECYL DIPHENYL PHOSPHATE

Submitted by:

FERRO CORPORATION
CLEVELAND, OHIO

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INTRODUCTION

Isodecyl diphenyl phosphate, CAS Registry Number 29761-21-5, is a general purpose plasticizer for most commercial resins including polyvinyl chloride and its copolymers, cellulose nitrate, cellulose acetate-butyrate, ethyl cellulose, polymethyl methacrylate and polystyrene. IDP is a clear, odorless liquid. The chemical structure, formula and identification numbers for Isodecyl diphenyl phosphate are given below:

CAS No: 29761-21-5
EINECS No: 249-828-6
EINECS Name: Isodecyl diphenyl phosphate
Molecular formula: $C_{22}H_{31}O_4P$
Molecular weight: 390.5 g/mole
Structural formula:

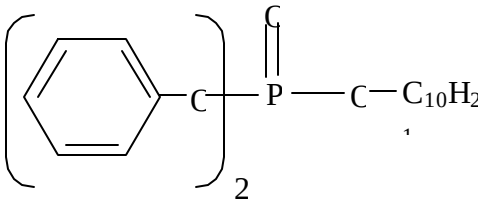

Table 1
PROPERTIES OF ISODECYL DIPHENYL PHOSPHATE

Property	**Value**
Melting point	<-50°C (pour point)
Boiling point (at atmospheric pressure)	>245°C (decomposes) @ 13.33 hPa (10mmHg)
Relative density	1.07-1.09 at 20°C
Vapour pressure	1.6×10^{-5} mmHg at 25°C
Water solubility	0.03-0.75 mg/l at room temperature
Octanol-water partition coefficient (log value)	5.44
Henry's law constant	0.062 Pa m^3/mole at 20°C
Flash point	465°F
Autoignition temperature	260°C
Explosivity	No data located

TEST PLAN RATIONALE

Ferro Corporation is committed to providing EPA with reliable data necessary to complete the SIDS screening matrix for the HPV voluntary challenge; however, Ferro Corporation is also committed to judicious use of research animal resources. As pointed out in its 2002 submission to EPA, Ferro Corporation would continue to attempt to obtain adequate documentation on existing studies of isodecyl diphenyl phosphate. This documentation has become available to Ferro, and the HPV Test Plan originally submitted has been revised to reflect reliance on existing studies.

Specifically, information has become available on the environmental effects, ecotoxicity and health effects of isodecyl diphenyl phosphate since the initial filing of this test plan. The information is in the form of toxicity and other testing reports, and is judged to be reliable[1]. Accordingly, Ferro is revising its HPV Test Plan for isodecyl diphenyl phosphate and presents this revised plan in Table 2.

Isodecyl diphenyl phosphate is of low acute mammalian toxicity. Acute oral LD50 values for isodecyl diphenyl phosphate are above current limit test values for this endpoint, i.e., > 5000 mg/kg, meaning isodecyl diphenyl phosphate would be considered "practically non-toxic" if it were a consumer product, which it is not. Repeat-dose oral testing in rodents has established that isodecyl diphenyl phosphate affects the liver but only at daily dietary doses of about 100mg/kg/day and 500 mg/kg/day. Subtle changes were seem in red blood cells parameters (hematocrit and MCV) at the lowest dose level, but these were unaccompanied by organ weight or structural changes of any type.

Reproductive organs were evaluated for adverse structural effects in the rodents subchronic toxicity study and found to be unaffected by isodecyl diphenyl phosphate treatment. Developmental toxicity was shown not to occur in a standard developmental toxicity/teratology study at the highest dose tested, 3000 ppm in the diet or about 200 mg/kg/day .

Isodecyl diphenyl phosphate did not produce gene mutation in bacterial or mammalian cells when tested with and without standard protocols employing exogenous metabolic activation systems. Chromosomal effects testing has not been performed on isodecyl diphenyl phosphate.

The environmental toxicity of isodecyl diphenyl phosphate has been described for effects in the freshwater crustacean Chironomus, algae, rainbow trout and fathead minnow. Biodegradation testing but not hydrolysis testing has been completed on isodecyl diphenyl phosphate as well.

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[1] Reliable according to the standards specified by Klimisch, et al., (Regulatory Toxicology and Pharmacology, 25, 1-5, 1997) or the EPA High Production Volume Challenge Program Guidelines For Determining the Adequacy of Existing Data Bases (http://www.epa.gov/chemrtk/datadfin/htm).

With the exception of hydrolysis testing and chromosome aberration testing, these data adequately provide results for the base set of environmental and human health effects endpoints identified by EPA in the HPA SIDS Level 1 data development screen. Accordingly, hydrolysis testing and chromosome aberration testing is proposed for isodecyl diphenyl phosphate.

TEST PLAN: ISODECYL DIPHENYL PHOSPHATE

Table 2 lists the HPV testing planned by Ferro Corporation for isodecyl diphenyl phosphate. These testes are:

Hydrolysis Testing OECD Test Method 111

In Vitro Mammalian Chromosome Aberration Testing OECD Test Method 473.

CONCLUSION

Isodecyl diphenyl phosphate sold or distributed in the U.S. by Ferro is of uniform composition. The material is used as an intermediate in chemical processing, principally of plastics. Existing test results, although dated in some cases, are reliable and entirely applicable to current assessments of isodecyl diphenyl phosphate. New testing would violate animal use goals without producing additional meaningful scientific information, and would thus also be unnecessarily burdensome.

With the exception of hydrolysis testing and chromosome aberration testing, Ferro proposes no additional testing of isdodecyl diphenyl phosphate. Existing studies, summarized in Appendix 1 account for the data requirements identified by EPA in the HPV voluntary data development program.

Table 2
ISODECYL DIPHENYL PHOSPHATE HPV TEST PLAN

HPV DATA ENDPOINT		PROPOSED DATA DEVELOPMENT METHOD
1. CHEMISTRY		
Melting Point	<-50 °C	No testing proposed
Boiling Point	>245°C @ 13.33 hPa (10mmHg)	No testing proposed
Vapor Pressure	1.6 X 10^{-5} mmHg @ 25°C	No testing proposed
Water Solubility	<0.08 mg/l @ 25°C	No testing proposed
Partition Co-Efficient	5.44	No testing proposed
2. ENVIRON-MENTAL FATE		
Photodegradation	Calculated fro AOPWIN v. 1.90 (EPISuit model v.3.10) Overall atm. rate constant: 41.978X10^{-12} cm^3/molec-sec, 1.5X10^5 molec/cm^3, 12 hr light	No testing proposed
Hydrolysis (Stability in Water)		Testing proposed: OECD 111 Hydrolyis
Biodegradation	Readily biodegradable 63% degraded after 28 days	No testing proposed
Fugacity Four compartment level III modeling	% in air = 7.7X 10^{-3} % in soil = 92.3 % in water = 0.51 % in sediment = 7.72	No additional modeling proposed
3. HEALTH EFFECTS		
Acute Toxicity	Rat oral LD50 = > 5000 mg/kg	No testing proposed
Repeat Dose Toxicity	90 day dietary study in rats LOAEL = 140 ppm (~9-10 mg/kg/day),	No testing proposed
Repro-Develop. Toxicity	Rat developmental toxicity NOAEL > 3000mg/kg/day	No testing proposed
Genetic Toxicity		
Bacterial mutation Test	Negative for mutation with and without activation	No testing proposed

Mammalian cell mutation test	Negative for mutation with and without activation	No testing proposed
Mammalian chromosome damage test		Testing proposed: OECD 473 In Vitro Mammalian Chromosome Aberration Test
4. ECOTOXICITY		
Fish	Rainbow trout LC50 = 7.6 mg/l Fathead minnow LC50 = 18 mg/l	No testing proposed
Midge	EC50 = 0.61 mg/l	No testing proposed
Algae	96-hour LC50 = 71 mg/l (based on chlorophyll conc.) 96-hour LC50 = 79 mg/l (based on cell number)	No testing proposed

APPENDIX 1

ROBUST SUMMARIES

ISODECYL DIPHENYL PHOSPHATE

CAS NUMBER : 29761-21-5

I. PHYSICAL-CHEMICAL ELEMENTS

Test Material: ISODECYL DIPHENYL PHOSPHATE
Type Melting Point
Value : <-50°C
Sublimation : No
Method : Unknown
Year: 2002
GLP: Unknown
Remarks: None
Quality : Not stated
Reliability: Reliable with restrictions
Reference: Ferro Corporation Technical Data Sheet No. 2311541C.

Test Material: ISODECYL DIPHENYL PHOSPHATE
Type Boiling Point
Value : >245°C @ 1.3.33 Pa (10 mmHg)
Decomposition : Yes
Sublimation : No
Method : Unknown
Year: 2002
GLP: Unknown
Remarks: None
Quality : Not stated
Reliability: Reliable with restrictions
Reference: Ferro Corporation Technical Data Sheet No. 2311541C.
Test Material: ISODECYL DIPHENYL PHOSPHATE
Type: Vapor Pressure
Value: $1.6X10^{-5}$ mmHg @ 25°C
Method: Unknown
GLP: Unknown
Year: Unknown
Remarks: None
Quality: Not stated
Reliability: Reliable with restrictions
Reference: Boethling, R. S. and Cooper, J. C., Res Rev, 94, 49-99, 1985.

Test Material: ISODECYL DIPHENYL PHOSPHATE
Type: Partition Coefficient
Value: Log Kow = 5.44
Method: Unknown
GLP: Unknown
Year: Unknown
Remarks: None
Quality: Unknown
Reliability: Reliable with restrictions
Saeger, VW., et al, Environ Science Technol. 13: 840-844, 1979

Test Material: ISODECYL DIPHENYL PHOSPHATE
Type: Water solubility
Value: <0.08mg/L @ 25°C
Method: Unknown
GLP: Unknown
Year: 2002
Remarks: None
Quality: Unknown
Reliability: Reliable with restrictions
Source: Ferro Corporation Technical Data Sheet No. 2311541C

II. ENVIRONMENTAL FATE AND ECOTOXICITY

Test Material: ISODECYL DIPHENYL PHOSPHATE
Study type: Aerobic biodegradation OECD Guideline 301B; Ready Biodegradability
Test concentrations: 20 mg/L
Test system: Activated sludge;
Duration of study: 28 days
Observations: Not provided
Study endpoint: CO_2 evolution
Results: 63% degraded after 28 days
Statistical analysis of study data: Not stated
Reliability: Reliable with restrictions
GLP: No
Reference: IUCLID Dataset for isodecylphenyl diphenyl phosphate. European Chemicals Bureau, European Commission, 2000.

Test Material: ISODECYL DIPHENYL PHOSPHATE
Study type: Aerobic biodegradation OECD Guideline 301B; Ready Biodegradability
Test concentrations: 30 mg/L
Test system: Activated sludge;
Duration of study: 28 days
Observations: Not provided
Study endpoint: CO_2 evolution
Results: 62% degraded after 28 days
Statistical analysis of study data: Not stated
Reliability: Reliable with restrictions
GLP: No
Reference: J. American Oil Chemists Society 50: 159, 1973

Test Material: ISODECYL DIPHENYL PHOSPHATE
Study type: Aerobic biodegradation OECD Guideline 302A
Test concentrations: 3 and 13 mg/L
Test system: Activated sludge;
Duration of study: 24 hours
Observations: Not provided
Study endpoint: CO_2 evolution
Results: 45-75% degraded after 24 hours
Statistical analysis of study data: Not stated
Year: 1979
Reliability: Reliable with restrictions
GLP: No
Reference: Saeger V. W., Hicks O., Kaley R. G., Michael P. R., Mieure J. P. and Tucker E. S. Environmental fate of selected phosphate esters. Environ. Sci. Technol., **13**, 840-844, 1979.

Test Material: ISODECYL DIPHENYL PHOSPHATE (S-148)
Study type: Acute toxicity
Species: Oncorhynchus mykiss
Test concentrations: Not stated
Duration of test material exposure: 96 hours
Study endpoint: 50% decrease in survival at 96 hours
Results: 96 hour LC50 was 7.6 mg/l
Statistical analysis of study data: Yes
Comment: LC50 values exceed water solubility of test material
Year 2002
Reliability: Reliable with restrictions
GLP: No
Reference: Ferro Product Description and Safety Data Sheet for Santicizer 148. Additives Division.

Test Material: ISODECYL DIPHENYL PHOSPHATE (S-148)
Study type: Acute toxicity
Species: Pimephales promelas
Test concentrations: Not stated
Duration of test material exposure: 96 hours
Study endpoint: 50% decrease in survival at 96 hours
Results: 96 hour LC50 was 18 mg/l
Statistical analysis of study data: Yes
Comment: LC50 values exceed water solubility of test material
Year 2002
Reliability: Reliable with restrictions
GLP: No
Reference: Ferro Product Description and Safety Data Sheet for Santicizer 148. Additives Division.

Test Material: ISODECYL DIPHENYL PHOSPHATE (S-148)
Study type: Acute toxicity
Strain: Chironomus tentans
Test concentrations: 5 concentrations
Controls: Medium (negative) and solvent
Duration of test material exposure: 48 hours
Study endpoint: 50% decrease in mobility at 48 hours
Observations: dissolved oxygen, pH, water hardness and temperature
Results: 48 hour EC50 = 0.61 mg/l (0.40 – 0.82)
Statistical analysis of study data: Yes
Comment: LC50 values exceed water solubility of test material
Reliability: Reliable with restrictions
GLP: No
Reference: Acute Toxicity of Santicizer -148 to Chironomus tetans. Monsanto Company Environmental Life Sciences. Report Number ES-82-SS-78, 1982.

Test Material: ISODECYL DIPHENYL PHOSPHATE (S-148)
Study type: Acute toxicity
Strain: Selenastrum capricornutum (green algae)
Test concentrations: triplicate cultures tested at 5 concentrations: 320, 100, 56, 32 and 10 mg/L
Controls: Medium (negative) and solvent (dimethylformamide)
Duration of test material exposure: 96 hours
Study endpoint: 50% decrease in cellular chlorophyll , and 50% decrease in cell number at 96 hours
Observations: cell number, chlorophyll concentration, pH of growth culture medium,
Results: 96 hour EC50 for cell survival was 71 mg/L with 95% CI of 8-624;
96 hour EC50 for decrease in chlorophyll concentration was 79 mg/l with 95% CI = 8-744
Statistical analysis of study data: Yes

Comment: LC50 values exceed water solubility of test material
Reliability: Reliable with restrictions
GLP: No
Reference: Toxicity of S-148 to the freshwater alga Selenastrum capricornutum. EG&G Bionomics Marine Research Laboratory, Report Number BP-79-4-61, April 1979, Toxicity of S-141 (BN-79-1384348-1d) to the fresh water alga Selanastrum capricornicum.

III. MAMMALIAN TOXICITY

Test material: ISODECYL DIPHENYL PHOSPHATE (Lot ATS-526)
Study type: Acute mammalian toxicity
Species: Rat
Strain: Not Stated
Sex: Male
Number of animals
per dose level: 10 per dose level, weight range 180-268g
Administration: Single dose, oral gavage in corn oil. Three dose levels: 5, 50 and 5000mg/kg
Observations: Body weight prior to dosing
Pharmacotoxic signs daily through day 14 post-dose
Survival
Results: Acute oral LD50 > 5000mg/Kg
Statistical analysis of study data: Yes
Reliability: Reliable with restrictions
GLP: Work conducted prior to inception of GLP regulations
Reference: Acute oral toxicity – rats. Ten compounds. Hazleton Laboratories, Inc., Vienna, VA., June, 1969.

Test material: ISODECYL DIPHENYL PHOSPHATE (Lot ATS-526)
Study type: Acute mammalian toxicity
Species: Rat
Strain: Not Stated
Sex: Male and female
Number of animals
per dose level: 11, weight range 200-220g
Administration: Single dose, oral gavage . Seven dose levels: 1000-15800mg/kg
Observations: Body weight prior to dosing
Pharmacotoxic signs daily through day 7 post-dose
Survival
Results: Acute oral LD50 > 15800mg/Kg; all animals survived treatment
Statistical analysis of study data: No
Reliability: Not Reliable
GLP: Work conducted prior to inception of GLP regulations

Reference: Acute oral and dermal toxicity and skin and eye irritation studies using Santicizer 148. Younger Laboratories, St.Louis, Mo., August, 1971

Test Material: ISODECYL DIPHENYL PHOSPHATE (S-148. Lot QL-25501)
Study type: Developmental toxicity study
Test animals: Pregnant female Charles River COBS rats, approx. 15 weeks old
Number of test groups; number of animals /group: Control and 3 test groups: 300, 1000 and 3000mg/kg/day; 25F/group
Route of administration: Oral by gavage on days 6-19 of gestation
Study design: Pregnant females treated daily during gestation days 6-19 followed by Cesarean section delivery of pups on GD 20. Evaluation of uterine contents, skeletal and soft tissue evaluation of pups.
Observations: Maternal observations – Daily for mortality behavior and appearance. Body weight on GD 0, 6,9,12,16 and 20. Gross examination of organs of the abdominal and thoracic cavity. Uteri from females that appeared nongravid were collected for evaluation.
Uterine contents observation – uterine wet weight, number and location of viable and nonviable fetuses, early and late implantation sites, and number of resorptions and corpora lutea.
Fetal observations – weight and examination for external malformations and variations, externally sexed, half of the fetuses were processed for soft tissue evaluation and the remaining half were processed for skeletal evaluation.
Results: One low-dose animal died during treatment. Dry red matter was reported around the mouth, nose and forelimbs of dams in all groups. Alopecia was reported for mid- and high-dose animals. The study director found no differences among treated and control mean maternal body weight measurements. No biologically meaningful differences were reported between treated and control groups for any uterine parameter; there was a slight but statistically significant increase in the number of postimplantation losses in the high-dose group, but this was considered unimportant since the mean number of viable fetuses in that groups was comparable to the control. Dwarfism was reported in several pups of two l litters in the mid-dose group. Dwarfism occurs spontaneously in the Charles River rat (4.3% litter historical control incidence at IRDC), but there was no occurrence of it in the concurrent control animals for this study. The study director concluded that here were no biologically meaningful differences or dose-related trends in the number of fetuses or litters with malformations or genetic or developmental variations in any of the treatment groups when compared to control groups.
NOAEL: Developmental toxicity NOAEL = >3000mg/kg/day
Statistical analysis of study data: Yes
Reliability: Reliable
GLP: Yes
Reference:. Teratology study in rats. IRDC study number IR-80-001. International Research and Development Corporation, Mattawan, MI. January, 1981

Test Material: ISODECYL DIPHENOL PHOSPHATE (Lot DC 5A83 2087982)
Study type: Repeated dose (90-days) toxicity study in rats
Test animals: Male and female Sprague-Dawley rats, approx. 5 weeks old at study initiation
Number of test groups: number of animals /group: Control and 3 test groups: 140, 1400 or 7000 ppm in the diet; 30M and 30F/group
Duration of test material treatment: 90 days
Route of administration: Oral dietary admixture
Study design: Animals received test or control diet for 90 days and then sacrificed.
Observations: Survival twice daily; general appearance, behavior, toxic and pharmacologic effects body weight and food consumption (weekly), urinalysis (7 parameters) hematology and clinical chemistry (18 parameters) at study week 6/7 and13/14, gross necropsy, organs weights (brain, kidneys, liver, testes with epididymides), histopathological analysis (30 tissues plus lesions) in high-dose and control animals. Liver from 2 high-dose and 2 control males was processed for and examined by electron microscopy. Reproductive tissue including ovaries, mammary gland, uterus (corpus and cervix), testes and epididymides were examined microscopically in the high-dose and control groups.
Results: One male (low dose) did not survive the study. No adverse behavioral effects were noted for the test animals. Body weight gain in the high- dose group and males and females was statistically-significantly suppressed. Food consumption was suppressed in a dose-related manner, with high-dose animals eating about 10% less food per day than controls (0.4-3.4% difference on a g/kg/day basis). RBC and MCV were reduced in a dose-related manner at the interim evaluation but increased at the terminal evaluation. The increases in these two parameters occurred in both sexes of each treated group. Hemoglobin and platelet counts were elevated at terminal sacrifice for high-dose females; depressed WBC was reported for all female test groups. Clinical chemistry changes indicate liver changes (elevated SGPT, cholesterol, phosphorous at terminal sacrifice). Urobilinogen and urinary bilirubin were elevated in high-dose animals or each sex – most prominently in males. Absolute and relative liver weights were increased in male and female mid-and high-dose rats. Relative (but not absolute) increases were reported for high-dose testes-brain weight and high-dose kidney-brain weight for female. No other treatment-related organ weight changes were reported. There were no differences between treated and control animals in gross lesions reported for the study. Hepatocellular hypertrophy (periportal region) was reported for high-dose females and mid- and high-dose males. Brown pigmentation accompanied the liver changes. Electron microscopy confirmed abnormal structural changes within hepatocytes, primarily increases in smooth endoplasmic reticulum and the presence of inclusion bodies.
NOAEL: A NOAEL could not be established for this study due to the changes observed in red and white blood cells. The LOAEL is 140 ppm in the diet (9-10mg/kg/day)
Statistical analysis of study data: Yes
Reliability: Reliable

GLP: Yes
Reference: Subchronic study of Santicizer -148 plasticizer administered in the diet to albino rats, study number 820160. Monsanto Company Environmental Health Laboratory, St. Louis, MO., February, 1986.

IV. GENETIC TOXICITY

Test Material: (S-148)
Lot QH-28641 BO 78-81
Study type: Microbial cell mutation assay
Testor strains: Salmonella typhimurium TA-1535, TA-1537, TA-1538, TA-98, TA-100
Saccharomyces cerevisiae D4
Number of concentrations tested: 5 plus solvent and positive controls (6 positive control compounds)
Exogenous metabolic activiation: Arochlor-induced rat liver microsome S-9
Route of administration: Plate incorporation assay
Cytotoxicity evaluation: Cell growth evaluated (qualitatively)
Study endpoint: Auxotrophic cell mutation
Results: Negative for mutagenicity with and without metabolic activation.
Statistical Analysis
Of study data: No
Reliability: Reliable
GLP: No, but data quality reviewed by contractor and study records (protocol, SOP's staff training, study raw data) maintained
Reference:. Litton Bionetics, Inc., Mutagenicity evaluation of S-141 in the Ames salmonella/microsome plate test. Kensington, Md., June, 1978

Test Material: (S-148)
Lot QH-28641 BO 78-85
Study type: Mammalian cell mutation assay
Testor strains: Fischer mouse lymphoma L5178Y line
Number of concentrations tested: 5 plus solvent (DMSO) and
positive controls (EMS and DMN)
Testing in duplicate cultures
Exogenous metabolic activiation: Arochlor-induced rat liver microsome S-9
Route of administration: Plate incorporation assay
Observations: Cell growth (percent), total viable colonies, total mutant colonies, relative cloning efficiency
Study endpoint: Specific locus forward cell mutation at the thymidine kinase locus
Results: Negative for mutagenicity with and without metabolic activation.
Statistical Analysis
Of study data: No
Reliability: Reliable

GLP: No, but data quality reviewed by contractor and study records (protocol, SOP's staff training, study raw data) maintained
Reference:. Litton Bionetics, Inc., Mutagenicity evaluation of S-148 in the mouse lymphoma forward mutation assay. Kensington, Md., August, 1978